HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2016 April 15.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2015 April 15; 68(0 3): S286–S296. doi:10.1097/QAI.0000000000000520.

Integrating Prevention Interventions for People Living With HIV Into Care and Treatment Programs: A Systematic Review of the Evidence

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Abstract

Introduction—This review assesses the impact of prevention interventions for people living with HIV on HIV-related mortality, morbidity, retention in care, quality of life, and prevention of ongoing HIV transmission in resource-limited settings (RLSs).

Methods—We conducted a systematic review of studies reporting the results of prevention interventions for people living with HIV in RLS published between January 2000 and August 2014. Standardized methods of searching and data abstraction were used.

Results—Ninety-two studies met the eligibility criteria: 24 articles related to adherence counseling and support, 13 on risk reduction education and condom provision, 19 on partner HIV testing and counseling, 14 on provision of family planning services, and 22 on assessment and treatment of other sexually transmitted infections. Findings indicate good evidence that adherence counseling and sexually transmitted infection treatment can have a high impact on morbidity, whereas risk reduction education, partner HIV testing and counseling, and family planning counseling can prevent transmission of HIV. More limited evidence was found to support the impact of these interventions on retention in care and quality of life. Most studies did not report cost information, making it difficult to draw conclusions about the cost-effectiveness of these interventions.

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The authors have no conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the official positions of the US Department of State Office of the US Global AIDS Coordinator and Health Diplomacy, the Centers for Disease Control and Prevention, the US Agency for International Development, or the Naval Health Research Center.

Conclusions—This evidence suggests that these prevention interventions, if brought to sufficient scale and coverage, can help support and optimize the impact of core treatment and prevention interventions in RLS. Further operational research with more rigorous study designs, and ideally with biomarkers and costing information, is needed to determine the best model for providing these interventions in RLS.

Keywords

HIV/AIDS; resource-limited settings; HIV prevention; people living with HIV; positive health; dignity; prevention

INTRODUCTION

Globally, an estimated 35 million people were living with HIV (PLHIV) at the end of 2013, of which 32.6 million live in low- and middle-income countries.[1] Expansion of antiretroviral treatment (ART) services for PLHIV has led to a 22% decrease in HIV-related mortality since 2009. Although the number of people newly infected with HIV continues to decline, an estimated 2.1 million individuals acquired HIV in 2013.[1] Assisting PLHIV to maintain good health and avoid transmission is essential to a sustainable effective HIV response.

Prevention interventions integrated into the routine HIV care offered in facility and community settings can both protect the health of PLHIV and promote shared responsibility for prevention of HIV transmission.[2] These interventions take a holistic approach to meeting the needs of PLHIV by offering a comprehensive range of behavioral and biomedical interventions aimed at reducing the morbidity and mortality experienced by HIV-positive individuals and reducing the risk of transmission to HIV-negative partner(s) and infants. They also provide the support that PLHIV need to protect their physical and mental health while equipping them with the knowledge and skills necessary to protect the health of their partner(s) and families. As such, these interventions promote the link between respecting the human rights of PLHIV to access comprehensive health services and engaging PLHIV as equal partners in efforts to curb the HIV epidemic.[2] Finally, these prevention interventions for PLHIV—also known as Prevention with Positives; Positive Prevention; or Positive Health, Dignity, and Prevention—provide a supportive foundation for optimizing high-impact prevention interventions including ART, prevention of mother-to-child transmission (PMTCT), male circumcision, and HIV testing targeted to individuals at highest risk of infection.

The US Government's President's Emergency Plan for AIDS Relief (PEPFAR) defines the minimum package of prevention interventions for PLHIV as including the following 5 components: (1) adherence counseling and support, (2) risk reduction education and condom provision, (3) HIV serostatus disclosure counseling and partner HIV testing and counseling (HTC), (4) family planning (FP) counseling and services, and (5) assessment and treatment of other sexually transmitted infections (STIs).[3] This package of services is consistent with guidelines issued by the World Health Organization.[4] Systematic integration of all 5 prevention interventions for PLHIV into existing HIV care and treatment programs in facility and community settings can improve PLHIV's access to the full range of services,

ensure that these services are consistently delivered and documented, and that services delivered meet the basic standards of quality necessary to achieve the desired outcomes.

Although evidence exists on the effectiveness of prevention interventions for PLHIV in US domestic settings,[5,6] the data from resource-limited settings (RLSs) are lacking.[7] Many donor agencies are experiencing reduced funding levels, requiring that resources be strategically prioritized to invest in high-impact evidence-based activities. The purpose of this systematic review is to summarize the evidence for the 5 prevention interventions for PLHIV in RLSs to provide guidance to national program managers and planners on how best to use their limited HIV prevention, care, and treatment resources to maximally impact the HIV epidemic. This article is part of a series of 12 systematic reviews published in this supplement that address the likely impact of HIV care and support interventions on the following clinical outcomes: (1) mortality, (2) morbidity, (3) retention in HIV care, (4) quality of life, and (5) prevention of ongoing HIV transmission. This article also describes data on the cost-effectiveness of the 5 prevention interventions, where available.

METHODS

Relevant literature was identified through database searches of PubMed, MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Sociological Abstracts, and African Index Medicus using a standard set of search terms (see the Introduction Paper for general search terms and Table 1 for intervention definitions and search terms). Search results were imported into EndNote X4, a bibliographic citation management software, and duplicate citations deleted. Article titles were then reviewed and clearly irrelevant citations removed. Any article that appeared to contain relevant information during these electronic searches was retrieved and the bibliography was searched for additional references. In addition, the bibliographies of relevant systematic reviews, meta-analyses, or current guidelines were also examined to identify potentially relevant articles. Once a pool of potentially eligible studies was created, the full-text article was retrieved. Final inclusion/exclusion of studies was based on a thorough reading of the full-text article by at least 2 study authors.

To be eligible for inclusion, articles had to (1) report on 1 of the 5 prevention interventions, (2) specifically target PLHIV or HIV-serodiscordant couples, (3) be conducted in a RLS (based on categories of low-income and lower-middle income economies as defined by the World Bank), (4) include a quantitative comparison of individuals or groups who received the intervention vs. those who did not, or a comparison of individuals or groups before and after receiving the intervention, (5) present data on at least 1 of the 5 outcomes of interest (mortality, morbidity, retention in care, quality of life, and prevention of HIV transmission), and (6) be published between January 1, 2000 and August 30, 2014. Articles were also included if they provided information on costing or cost-effectiveness of 1 of the 5 prevention interventions in RLSs. Only articles published in English in a peer-reviewed journal were included in the review. Articles published in other languages and/or conference abstracts were not included.

A systematic process was then used to assess the quality of published studies and the likely impact of each intervention on the 5 clinical outcomes. Each article was read in its entirety and data were abstracted using a systematic coding form. Information abstracted from each article included study characteristics (eg, design, time period conducted, setting, and number of participants) and key findings. For each article, authors rated the internal validity of the study (eg, amount of bias, confounding, attrition, and other factors that could affect the interpretation of the study findings) and the external validity or generalizability of the study findings. For each article, the overall quality of evidence was rated as strong, medium, or weak. Once all articles were reviewed, the overall quality of evidence and expected impact of the intervention by outcome was determined based on the magnitude of effect demonstrated in individual studies, the quality of the body of evidence (all included studies), and consistency across all studies reviewed. The overall quality of evidence was then rated as good, fair, or poor and the expected impact of the intervention on each of the 5 clinical outcomes was rated as high, moderate, low, or uncertain. See the introductory article in this supplement for more details on how the various ratings were defined and determined.[8]

RESULTS

Of the 4132 articles identified through the search, many were eliminated based on a title and abstract review (Fig. 1). Three hundred eighty-seven abstracts were selected for review, of which 158 full-text articles were further evaluated. Of those, 92 were deemed to meet the eligibility criteria including 24 articles related to adherence counseling and support, 13 on risk reduction education and condom provision, 19 on disclosure and partner testing, 14 on provision of FP services, and 22 on STI assessment and treatment. The outcomes addressed within each intervention are summarized in Figure 1. These articles were used to generate the observations and conclusions described below and in Tables S1–S3 (see Supplemental Digital Content, http://links.lww.com/QAI/A646).

Adherence Counseling and Support

Twenty-four studies reporting on adherence counseling and support interventions were identified (see Table S2, Supplemental Digital Content, http://links.lww.com/QAI/A646).[9–31,93] Two of the studies reported mortality as an outcome,[9,10] 22 reported morbidity,[9–30] 1 on retention in care,[19] 2 on quality of life,[15,20] and 1 on prevention of HIV transmission,[31] with some studies reporting on multiple outcomes. One article included information on the costs associated with providing adherence counseling and support.[93] Most of the intervention studies were conducted in sub-Saharan Africa (19), followed by Asia (3) and South America (2).

Only 2 studies, with conflicting results, reported the effect of adherence counseling and support on mortality.[9,10] In a randomized control trial from South Africa, survival was significantly better with directly observed therapy compared with self-administered therapy.[9] However, another randomized control trial from Nigeria found no significant difference in mortality after 48 weeks of follow-up comparing partnerassisted therapy and standard of care.[10] Thus, the overall body evidence for the effect of adherence counseling

and support interventions on mortality is poor and the expected impact remains uncertain (see Table S3, Supplemental Digital Content, http://links.lww.com/QAI/A646).

In contrast, this review found good evidence that adherence counseling and support interventions can have a high impact on improving HIV-related morbidity measured through both adherence (self-report or through pill counts)10,11,13,16,20,21,23,24 and virologic suppression.[10,12,13,15,17] Effective interventions include provider-delivered adherence counseling,[13,15,16,24] food supplementation,[11] treatment supporters,[10] adherence support from community health workers,[12,20,21] and mobile phone text messages.[17,23] The evidence for directly observed therapy was mixed with some studies finding a positive association with adherence and clinical outcomes[22,26] and other studies finding no association.[9,14]

Only 1 study, with null findings reported the effect of adherence support on retention in care.[19] In a trial from Tanzania, Mugusi et al found no difference in the number of patients who stopped attending the clinic for more than 3 months comparing participants who received regular adherence counseling, those who received regular counseling plus a calendar, and those who received regular counseling and a treatment assistant.[19] Overall, the body of evidence on the effect of adherence counseling on retention in care is poor and the overall impact remains uncertain.

Two studies, both with weak designs, found that adherence counseling and support was associated with improvements in the quality of life experienced by PLHIV including the amount of social support they received and a reduction in their depressive symptoms.[15,20] These studies provide a fair amount of evidence that adherence counseling can have a moderate impact on the quality of life among HIV-infected adults, although additional research is needed.

Finally, only 1 small study examined the effect of adherence counseling on prevention of HIV transmission.[31] This study, conducted among 60 women living with HIV (WLHIV), found that motivational interviewing was associated with higher rates of self-reported adherence and condom use.[31] However, given the paucity of data, the overall body of evidence on the effect of adherence counseling on prevention of HIV transmission is poor and the expected impact remains uncertain. Additional research will be needed to determine if adherence counseling can lead to reductions in HIV risk behavior.

The cost-effectiveness of providing adherence counseling and support was reported in 1 cohort study from South Africa (see Table S3, Supplemental Digital Content, http://links.lww.com/QAI/A646). This study, conducted among 6833 HIV-infected adults, found that increasing patients' ART adherence was associated with reduced hospitalization costs and lower mean monthly direct health care costs.[93] Additional information is needed to assess the cost-effectiveness of the specific interventions for providing adherence counseling and support described above.

Risk Reduction Education and Condom Provision

Thirteen studies were identified that reported the effectiveness of risk reduction education interventions (see Table S1, Supplemental Digital Content, http://links.lww.com/QAI/

A646).[32–44] Two of the studies reported morbidity as an outcome,[32,33] 2 reported quality of life,[34,35] and 13 reported prevention of HIV transmission.[32–44] Most of the studies were conducted in sub-Saharan Africa (11), followed by South America (1) and Asia (1).

Only 2 studies, reporting conflicting results, reported the impact of risk reduction education on morbidity. A small randomized control trial conducted among 120 HIV-positive pregnant women attending primary care clinics in South Africa found that a 4-session risk reduction and coping intervention was associated with a significant reduction in STI incidence.[33] However, a much larger randomized control trial in South Africa conducted among 1480 pregnant women found no intervention effects on STI incidence.[32] Given these mixed findings, the evidence for the ability of risk reduction interventions to reduce STI incidence and other biologic outcomes is poor and the impact remains uncertain.

Two studies, a randomized control trial and an observational study, reported the effect of a group-based intervention on the quality of life experienced by PLHIV. Both studies found improved coping and social support after a risk reduction intervention.[34,35] These studies provide fair evidence that risk reduction interventions may moderately improve the quality of life for PLHIV, although additional research is needed.

Although the evidence is mixed, 13 studies including several well-conducted randomized control trials and observational studies indicate that risk reduction interventions are associated with lower rates of self-reported sexual risk behaviors.[32–44] This is particularly true when the education is provided during multiple high-intensity sessions.[35–41,43] Only 1 randomized controlled trial focused on alcohol reduction counseling. This study, conducted among PLHIV reporting hazardous or binge drinking in Kenya, found that cognitive-behavioral therapy was associated with fewer drinking days and fewer mean drinks per day.[42] The collective findings from the 13 studies provide good evidence that risk reduction interventions can have a high impact in reducing self-reported sexual risk behavior and preventing onward transmission of HIV.

Disclosure Counseling and Partner HTC

Nineteen studies were identified that reported the effectiveness of interventions to increase partner HTC (see Table S2, Supplemental Digital Content, http://links.lww.com/QAI/A646).[45–59,94–97] Two of the studies reported retention in care as an outcome,[45,46] 2 reported quality of life,[47,48] and 15 reported prevention of HIV transmission.[45,46,48–59,94] In addition, 3 studies included information on the costs associated with providing partner HTC.[95–97] All 16 intervention studies were conducted in sub-Saharan Africa.

Within antenatal programs, 2 studies provide fair evidence that couples and index partner testing can lead to improved retention of the pregnant mother in PMTCT programs.[45,46] Women who received couples HTC were more likely to use nevirapine[45] and to deliver in a hospital and return for the 18-month postnatal follow-up visit[46] than women who received individual HTC. However, because only a few studies included retention as an outcome, the expected impact of couples HTC on improving retention in care remains uncertain.

Two studies found no significant association between partner testing and improved quality of life among HIV-infected pregnant women attending antenatal clinics.[47,48] In a randomized control trial from Tanzania, there was no significant difference in rates of depression comparing a nurse-facilitated psychosocial support group to standard of care.[47] A study from Zambia found no significant difference in the reported number of adverse events between women who tested as a couple compared with those who tested individually.[48] Although this study provides some reassurance that couples HTC is not associated with an increased risk of experiencing an adverse event, additional research is needed. Overall, the body of evidence for the effect of couples and partner HTC on quality of life is poor and the expected impact remains uncertain.

Fifteen studies included prevention of onward HIV transmission as an outcome.[45,46,48–59,94] In 6 of these studies, couples and partners HTC was associated with better uptake of interventions for PMTCT,[45,50,56] reduced rates of vertical transmission,[49] and reductions in self-reported sexual risk behavior[46,58] among pregnant women attending antenatal services. Six other studies reported innovative strategies to increase uptake of partner HTC outside of antenatal settings.[51,53–55,57,94] A study in Uganda found that counselor-facilitated disclosure was associated with increased disclosure rates among HIV-infected adults in a serodiscordant relationship.[54] In addition, home-based index partner testing was associated with increased uptake of couples and partner HIV testing in Uganda[55,57] and Kenya.[94] Partner notification and contact tracing was also associated with increased rates of partner HIV testing among individuals newly diagnosed with HIV in Malawi[51] and Cameroon.[53] In the study from Cameroon, an average of 3.2 index cases were interviewed for every 1 case of HIV identified, suggesting that partner notification strategies may be a highly effective strategy for identifying new cases of HIV.[53] The remaining 3 studies found null effects for the association between couples and partner HTC and prevention of HIV transmission.[48,52,59] Altogether, these studies provide good evidence that partner notification, contact tracing, and various forms of indexpatient HTC can have a high impact on preventing both vertical and horizontal transmission of HIV.

Three studies reported cost-effectiveness information. In 1 analysis from a prospective cohort study, the total program cost for couples HTC was more expensive (US $44,013) than individual HTC (US $42,528), but couples HTC averted a greater number of infant infections (91 vs. 88).[95] A study from Malawi compared the cost-effectiveness of 3 partner notification strategies: provider notification (provider attempts to notify indexes' locatable partners), contract notification (index given 1 week to notify partners then provider attempts notification), and passive referral (index is encouraged to notify partners, standard of care). The costs per new case identified were $36 for provider notification, $18 for contract notification, and $8 for passive referral and the costs per partner tested were $19 (provider), $9 (contract), and $4 (passive).[96] Similarly, findings from another costing study indicate that contact tracing could be a cheaper approach to detecting an undiagnosed HIV infection than both client-initiated and provider-initiated testing in rural settings with low-to-moderate HIV prevalence.[97]

FP Counseling and Services

Fourteen studies reported the provision of FP education and services (see Table S2, Supplemental Digital Content, http://links.lww.com/QAI/A646).[60–71,98,99] One study reported morbidity,[61] whereas 12 studies reported prevention of HIV transmission.[60–71] In addition, 2 studies reported the costs associated with providing FP services.[98,99] All 12 intervention studies were conducted in sub-Saharan Africa. FP interventions included a facilitated referral model,[61] integration of FP services into HIV clinical care,[62,64–68] an education video to promote long-acting methods of contraception,[63,70,71] and group education sessions.[69]

Only 1 study reported the morbidity associated with hormonal contraceptive use among WLHIV.[60] In this study, clinical disease progression was more common among hormonal contraceptive users compared with intrauterine device (IUD) users.[60] Given the paucity of data, the overall body of evidence for the effect of contraceptive use on morbidity is poor and the expected impact remains uncertain (see Table S3, Supplemental Digital Content, http://links.lww.com/QAI/A646).

Prevention of unintended pregnancy through voluntary contraceptive use is a key component of efforts to prevent mother-to-child HIV transmission. Twelve studies reported the effects of FP counseling on contraceptive uptake and prevention of unintended pregnancy.[60–71] Most of these studies reported significant increases in contraceptive uptake as a result of the intervention,[61,62,65–68,70,71] although 2 studies reported null effects.[64,69] Of the 4 studies that included pregnancy incidence as an outcome, 2 found a significant reduction in pregnancy incidence,[68,71] and 2 found no change in pregnancy incidence as a result of the intervention.[62,65] Taken together, these studies provide good evidence that FP interventions can have a high impact on improving contraceptive uptake but the impact on pregnancy incidence remains uncertain.

Cost analysis indicates that preventing unintended births among HIV-infected women with FP services would cost US $63 per birth averted globally.[98] In a randomized control trial from Kenya, integration of FP services into HIV clinical care was associated with an average marginal cost of US $841 per site, US $48 per female patient, and US $1368 for each pregnancy averted.[99]

STI Assessment and Treatment

Twenty-two studies reported the assessment and treatment of other STIs among individuals living with HIV (see Table S2, Supplemental Digital Content, http://links.lww.com/QAI/A646).[72–92,100] Ten studies reported morbidity,[72–81] whereas 16 reported prevention of HIV transmission.[73,76–78,81–92] In addition, 1 study reported the costs associated with STI treatment.[100] Fourteen of the intervention studies were conducted in sub-Saharan Africa, 3 in South America, and 4 at multiple sites.

A systematic review of 37 studies highlights the degree to which PLHIV are coinfected with other STIs.[101] In this review, the overall mean point prevalence for confirmed STI was 16.3% (SD = 16.4), and the median STI prevalence in PLHIV was 12.4%. The most common STIs were trichomoniasis (median: 18.8%), syphilis (9.5%), gonorrhea (9.5%), and

chlamydia (5%). STI prevalence was greatest at the time of HIV diagnosis but once enrolled in care, there was no difference in STI prevalence between PLHIV receiving and not receiving ART.

Ten studies reported the effect of STI assessment and treatment on HIV-related morbidity.[72–81] These studies include several well-conducted randomized control trials and observational studies that provide good evidence that STI treatment can reduce the morbidity experienced by PLHIV. A single 2 g dose of metronidazole was found to effectively treat *Trichomoniasis vaginalis* in both HIV-positive and negative women.[72] However, persistent infection was associated with being on a nevirapine-based ART regimen and having a concurrent bacterial vaginosis infection.[72] Similarly, penicillin therapy appeared to be effective at treating incident cases of syphilis in HIV-serodiscordant couples, irrespective of HIV status.[74] Although treatment of HSV-2 with nucleoside analogs such as acyclovir and valacyclovir has been shown to reduce the occurrence of genital ulcers among PLHIV,[73] it is unclear if these medications impact ulcer healing.[77,78] Acyclovir treatment, however, may reduce the risk of HIV disease progression (defined as CD4 <200 cells/mm^3 or WHO clinical stage 4) by as much as 16%.[75,79,80]

Sixteen studies reported the effect of STI assessment and treatment on the prevention of HIV transmission,[73,76–78,81–92] including 15 studies on how coinfection with another STI can impact the infectiousness of HIV[76–78,81–92] and 1 study directly assessing the impact of HSV-2 treatment on HIV incidence.[73] Two of these studies indicate that genital HSV-2 is associated with increased cervicovaginal, seminal, and plasma HIV-1 RNA viral load concentrations.[76,81] Treatment of HSV-2 with valacyclovir and acyclovir seems to reduce the frequency of lesional HIV-1 RNA shedding[77,78,84] and plasma HIV-1 viral load concentrations.[73,83,85,89,90] These drugs were also associated with reductions in seminal[78,91] and rectal[92] HIV-1 RNA plasma detection in men but not the frequency of cervical–vaginal shedding in women.[78,85] A large multisite intervention trial conducted among HIV-serodiscordant couples failed to find an association between acyclovir treatment and a reduction in the risk of HIV transmission.[73] However, the study did find a reduction in plasma HIV-1 RNA levels and a 73% reduction in the occurrence of genital ulcers as a result of HSV-2 treatment.[73] Similarly, treatment of T. vaginalis was not associated with reductions in genital tract viral load.[82,87] Taken together, these findings provide good evidence that STI assessment and treatment is likely to have a low impact on preventing HIV incidence at either the individual or population level.

One study from South Africa presented cost information on HSV-2–suppressive therapy.[100] The costs of this therapy were estimated to be about US $737 per life year gained (95% confidence interval: $373 to $2489) if ART eligibility criteria were set at CD4 count <350 cells per microliter. These costs compare favorably with the estimated cost-effectiveness of ART in South Africa (~US $1200 per life year gained), suggesting that HSV-2–suppressive therapy may be a cost-effective intervention for delaying HIV disease progression among PLHIV not yet eligible for ART.

DISCUSSION

This systematic review summarizes the evidence for 5 interventions that comprise the minimum package of prevention interventions for PLHIV as defined by PEPFAR.[3] These interventions include (1) adherence counseling and support, (2) partner HTC, (3) FP counseling and services, (4) risk reduction education, including an alcohol screening, and condom provision, and (5) assessment and treatment of other STIs. Findings from this review provide good evidence that adherence counseling and support and STI assessment and treatment can have a high impact on the morbidity experienced by PLHIV enrolled in HIV care. In addition, this review found good evidence that risk reduction education, partner HTC, and FP counseling can prevent onward transmission of HIV. More limited evidence was found to support the efficacy of these interventions at impacting mortality, retention in care, and quality of life. Most studies did not report cost information, making it difficult to draw conclusions about the cost-effectiveness of these interventions.

These findings are consistent with a randomized control trial conducted in Tanzania, Kenya, and Namibia, which found that integrating this package of prevention services into the routine care offered to PLHIV was associated with lower rates of unprotected vaginal sex and higher rates of contraceptive use (P. Bachanas, personal communication, February 19, 2015). Further research is needed, however, to determine the synergistic effects of providing all 5 of the prevention interventions together as a package instead of 5 separate interventions.

Programmatic Considerations

Results of this review indicate that prevention interventions for PLHIV can be effectively delivered by health care providers in health facilities[5,29] and by lay or peer counselors in clinic and community settings.[37,43] Many implementation challenges remain, however, to ensure that all PLHIV have access to effective prevention services. First, coordination and collaboration across multiple disciplines including care and treatment, prevention, and HTC will be required to integrate HIV prevention into the routine care offered to PLHIV in both clinic and community settings. Collaboration with other key stakeholders including health care workers with “real-world” implementation experience, technical advisors from international agencies, and PLHIV will also be necessary to ensure the continuity and sustainability of prevention programs for PLHIV. National HIV prevention, care, and treatment guidelines and policies may need to be revised to include prevention activities for PLHIV. In addition, national plans for implementation of prevention interventions for PLHIV may need to be developed. These plans should include clear and measurable objectives for integration, articulate plans for training facility and community-based service providers, describe methods for documenting and reporting provision of prevention interventions for PLHIV, and include strategies for ensuring that prevention interventions are implemented with high quality and fidelity.

At the facility and community level, programs will need an adequate number of trained staff to deliver prevention interventions for PLHIV. In addition, task-shifting some responsibilities to lay counselors, expert patients, and PLHIV volunteers is a potentially cost-effective and supportive model for delivering prevention counseling and partner and

couples testing to HIV-positive patients. With appropriate supportive supervision from health care providers, lay counselors and patient volunteers can provide more in-depth counseling on prevention services and help clients set and meet prevention goals. Programs will also need to ensure a regular supply of necessary commodities including condoms, STI drugs, contraceptives, and HIV rapid test kits to ensure that providers are able to deliver prevention interventions for PLHIV. Finally, it is important that providers are able to document and monitor the prevention services they deliver to patients. Revising existing registers and patient records may be necessary to allow documentation of these services. Programs should also be encouraged to use their routine program data to continually improve the quality of services they offer to their HIV-infected clients.

Research Gaps

Prevention interventions were most effective when targeted to patients known to be at risk for nonadherence and/or continued high-risk behavior and when a focus on developing practical management skills was included as part of the intervention.[8,102] There is now a need to identify how to tailor these prevention interventions to settings and populations in which HIV transmission is occurring. This includes patients who experience difficulty in reducing their HIV risk behaviors, young people (aged 15–24) who account for nearly one-third of individuals estimated to be newly infected with HIV globally,[1] and key populations including men who have sex with men, sex workers, transgender people, and people who inject drugs.

Many of the FP interventions were associated with significant increases in uptake of highly effective contraceptive methods. These uptake rates, however, did not always translate into reduced incidence of unintended pregnancy primarily because of high levels of discontinuation, method switching, and user failure. Further operational research is needed to determine strategies for helping women maintain their contraceptive method of choice or to safely switch methods without compromising the efficacy of the current method to prevent unintended pregnancy.

In addition, concerns have been raised about hormonal contraceptive use among women living with and at risk for HIV.[103] Several systematic reviews indicate that hormonal contraceptive use is safe in WLHIV and is not associated with HIV disease progression,[104,105] female-to-male HIV transmission,[106] or reduced ART efficacy.[107] However, the data on hormonal contraceptive use and the risk of HIV acquisition among HIV-negative women in serodiscordant relationships are more difficult to interpret. Some studies indicate that progestin-only injectables are associated with an increased HIV-acquisition risk, whereas other studies report nonsignificant findings.[108] A large clinical trial to provide further evidence on this issue is being planned. In the meantime, women at high risk for HIV acquisition, including women in serodiscordant relationships, should be counseled about the importance of using condoms in addition to progestin-only injectables to protect against unintended pregnancy and the risk of acquiring and transmitting HIV and other STIs.[109]

Although several studies found that treatment of HSV-2 seems to reduce the frequency of lesional HIV-1 RNA shedding[77,78,84] and plasma HIV-1 viral load,[73,83,85,89,90] a large

multisite intervention trial failed to find an association between daily acyclovir treatment and reduced risk of HIV transmission.[73] These findings highlight the unknown benefits of suppressing HIV in the genital tract, because the exact mechanism by which HIV transmission occurs, including the concentration of HIV required for transmission, remains unknown.[78] Further research in this area is needed to determine what role, if any, that STI treatment may play in preventing HIV transmission.

Limitations of the Current Review

The ability to draw conclusions regarding the effectiveness of prevention interventions for PLHIV is complicated by the fact that these interventions varied widely in terms of target populations (eg, men, women, couples), intensities, modalities (provider-delivered, counselor-delivered, delivered to individuals, delivered to groups, etc.), and indicators (eg, condom use at last sex vs. condom use during the past 3 months, self-reported adherence using a visual analog scale vs. pill counts, etc.). The lack of standard indicators limits the ability to compare findings across studies and to draw conclusions regarding the strength of the evidence base.

Furthermore, weak study designs and an overreliance on self-reported data limit the generalizability of the findings. Further operational research, with more rigorous study designs and ideally with biomarkers, is needed to determine the best model for providing HIV prevention services to PLHIV in both facility and community settings. These studies should answer questions related to “how” services should be delivered, “who” should deliver these services, and “where” to reach PLHIV with these services including those traditionally underserved in facility-based settings (eg, young men, sex workers, men who have sex with men, etc.). In addition, delivery of prevention interventions for PLHIV in communities has not been rigorously evaluated and community-based programs have not been brought to scale.

Finally, most studies included in this review did not report cost information. As a result, it is difficult to determine the cost-effectiveness of these prevention interventions and services. Adherence counseling and support and STI assessment and treatment were associated with improved clinical outcomes including achievement of viral suppression and prevention of treatment failure. Interventions that reduce treatment failure are likely to be cost saving since they reduce the need for more expensive second-line antiretroviral medications and prevent the costs associated with treating opportunistic infections. To test this premise, future studies should include a costing component to determine whether these interventions are cost-effective.

CONCLUSIONS

In summary, there is good but not perfect evidence supporting each of the 5 interventions included in the minimum package of prevention interventions for PLHIV. Adherence counseling and support and STI assessment and treatment were associated with positive impacts on the morbidity experienced by PLHIV. In addition, risk reduction education, partner HTC, and FP counseling had positive impacts on preventing both horizontal and vertical transmission of HIV. This evidence suggests that these interventions, if brought to

sufficient scale and coverage, can help support and optimize other high-impact interventions (eg, HTC, treatment as prevention, and PMTCT). Further operational research with more rigorous study designs, and ideally with biomarkers and costing information, is needed to determine the best model for providing these prevention services to PLHIV in RLSs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Gail Bang and Emily Weyant for their assistance with the literature search for this review, Margo Sloan and Kelly Woodland for their help in reading and reviewing articles for possible inclusion, and Naomi Bock and Janet Moore for their thoughtful suggestions on how to improve the manuscript.

Supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) through the US Department of State Office of the US Global AIDS Coordinator and Health Diplomacy, the US Centers for Disease Control and Prevention, the US Department of Defense, and the US Agency for International Development.

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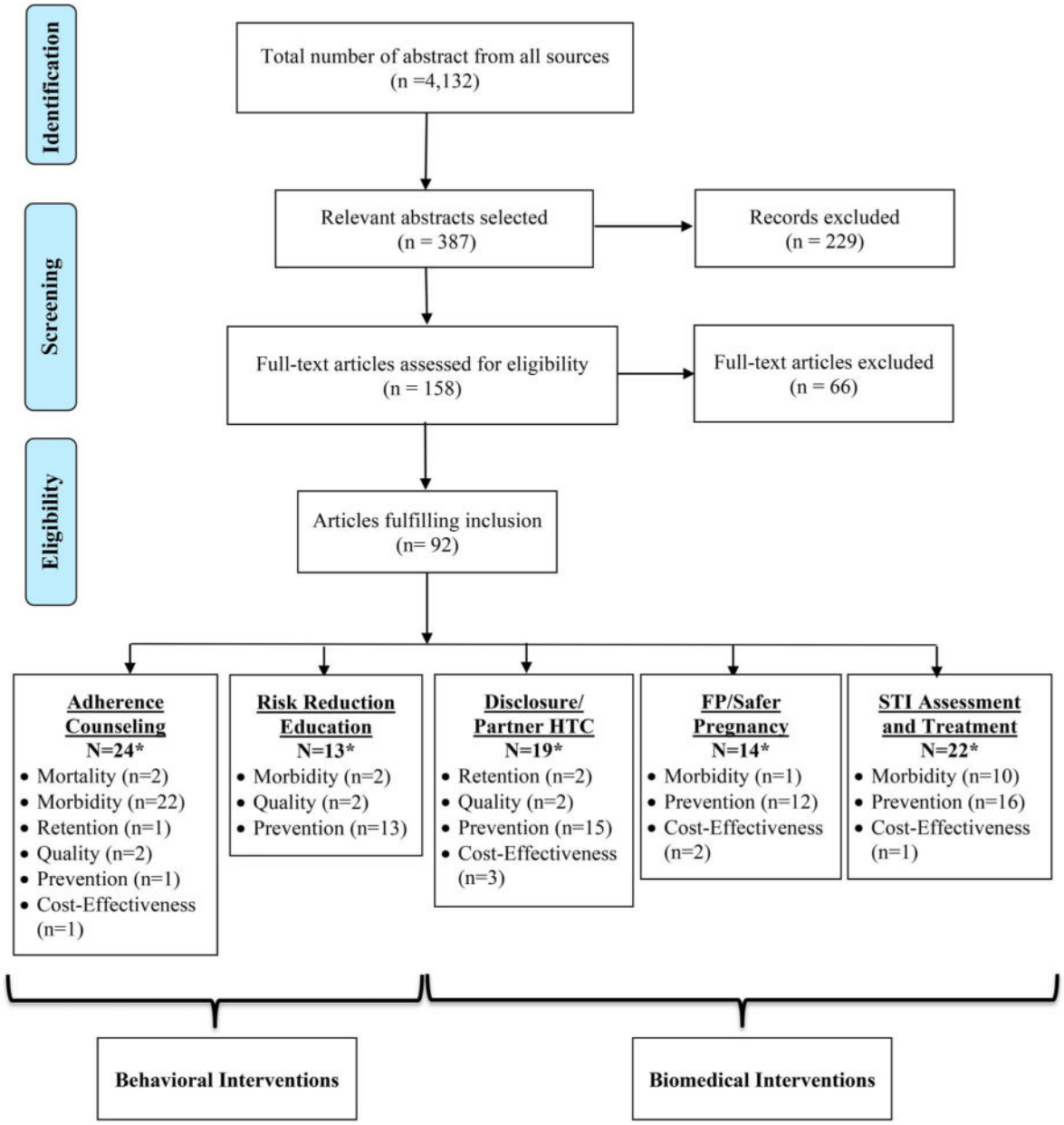

FIGURE 1.

Disposition of citations during the search and screening process in the systematic review of prevention interventions for people living with HIV in RLSs. *Some articles reported multiple outcomes.

TABLE 1

Intervention Definitions and Key Word Search Terms for Prevention Interventions for PLHIV

Intervention	Definition	Key Word Search Terms
Prevention interventions for PLHIV	A package of behavioral and biomedical HIV prevention interventions offered to PLHIV to prevent HIV-related morbidity and mortality, reduce onward transmission of HIV, and retain PLHIV in HIV care and treatment services	Positive prevention + HIV Prevention with Positives + HIV Positive health, dignity, and prevention
Adherence counseling and support	Interventions that support PLHIV to maintain optimal levels of adherence to prophylactic medications (eg, cotrimoxazole, isoniazid) and/or therapeutic regimens (eg, antiretrovirals)	HIV positive + adherence counseling PLHIV + adherence counseling
HIV serostatus disclosure counseling and partner HTC	Offering counseling to PLHIV on how they can safely disclose their HIV status to their sex partner(s) and how they can get their partner (s) tested for HIV. Partner testing can be integrated into other clinical services accessed by PLHIV (eg, antenatal, HIV care and treatment, TB) or offered through home- or community-based approaches	HIV positive + disclosure counseling PLHIV + disclosure counseling HIV + index partner testing HIV + couples testing and counseling
FP counseling and services	Assessing the reproductive intentions and fertility desires of PLHIV and then providing, as indicated, either FP counseling and contraceptives (either directly or through referral) OR safer pregnancy counseling and referral to PMTCT services	HIV positive + safe pregnancy counseling HIV positive + FP PLHIV + safe pregnancy counseling PLHIV + FP
Risk reduction education and condom provision	Ongoing counseling offered to PLHIV to support them in reducing their HIV risk behavior. Counseling typically includes messages on correct and consistent condom use at every sexual encounter, reducing number of sex partner(s), and alcohol reduction/elimination. In addition, PLHIV should be provided with an adequate supply of condoms (male or female) at every encounter with a provider or counselor in either a facility or community setting	PLHIV + safer sex HIV positive + safer sex Risk reduction counseling + PLHIV Risk reduction counseling + HIV positive HIV positive + condom distribution PLHIV + condom distribution Alcohol counseling + PLHIV Alcohol counseling + HIV positive
STI assessment and treatment	Assessing PLHIV for the signs and symptoms of other STIs [eg, vaginal/penile discharge, genital ulcers, and (for women) abdominal pain] and providing syndromic management according to national treatment algorithms for all patients who report symptoms and/or where symptoms are detected during a genital examination	PLHIV + STI assessment HIV positive + STI assessment PLHIV + syndromic management HIV positive + syndromic management PLHIV + STI treatment HIV positive + STI treatment